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DEVELOPMENT AND EVALUATION OF CLINICAL PROTOCOL FOR BREASTFEEDING AFTER GENERAL ANESTHESIA

by

Lacey Rae Gibson

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A DNP Project Submitted to the Faculty of the

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GRADUATE COLLEGE

As members of the DNP Project Committee, we certify that we have read the DNP project prepared by *Lacey Rae Gibson*, titled *Development and Evaluation of Clinical Protocol for Breastfeeding After General Anesthesia* and recommend that it be accepted as fulfilling the DNP project requirement for the Degree of Doctor of Nursing Practice.

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Final approval and acceptance of this DNP project is contingent upon the candidate's submission of the final copies of the DNP project to the Graduate College.

I hereby certify that I have read this DNP project prepared under my direction and recommend that it be accepted as fulfilling the DNP project requirement.

Sarah Torabi — Date: January 24, 2019
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And to my amazing family and friends, whose unconditional love and support for my boys and I made this dream come true – my deepest gratitude. It indeed takes a village to raise a child, thank you for raising us!

DEDICATION

To Jackson & Jameson, my loves. Your smiles made my struggles fade. Your hugs gave me the strength to go on. Thank you for being my biggest cheerleaders on this crazy journey. May you realize that there is no limit to what you can achieve!

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ABSTRACT

Inconsistent post-anesthetic advice imparted to breastfeeding mothers leads to unnecessary weaning or premature abandonment of nursing. This Doctoral of Nurse Practice (DNP) project set out to identify evidence-based research regarding post-anesthetic advice to communicate to breastfeeding mothers from their anesthesia providers. The first phase of the project involved the systematic development of a Clinical Practice Guideline (CPG) based on current evidence in the literature. The second phase of the project was the appraisal of the developed CPG by an interdisciplinary panel utilizing the AGREE II instrument. The overall quality of the developed guideline resulted in a combined score of 92%, representative of a high-quality guideline. Appraiser's judgment concerning recommended use of the developed guideline resulted with an answer of 'Yes' to the recommended use of the guideline. The overwhelming evidence suggests that drugs administered to a breastfeeding mother during the perioperative period are not harmful and will not precipitate adverse outcomes in the healthy breastfed infants (Dalal, Bosak, & Berlin, 2014). A breastfeeding mothers return to baseline mentation and strength, suggest drug redistribution from plasma and milk, and termination of drug action (Cobb et al., 2015). Mothers are encouraged to continue breastfeeding and disregard the past recommendation to "pump and dump." The American Academy of Pediatrics Committee on Drugs surmises, "*The benefits of breastfeeding outweigh the risk of exposure of most therapeutic agents via breastmilk*" (Sachs, 2013, p. 805).

INTRODUCTION

Inconsistent and often conflicting post-anesthetic advice imparted to breastfeeding mothers leads to unnecessary weaning or premature abandonment of nursing. The information in regards to the resumption of breastfeeding and milk discards can vary depending on anesthesia provider opinion, medical facility protocol, or the favored medically endorsed guideline. Furthermore, anesthesia providers, hospitals, and patients may rely on conservative and often restrictive recommendations given by drug manufacturers that may not accurately reflect conditions for lactating women and the transfer of anesthesia and analgesia medications into breast milk (Cobb, Liu, Valentine, & Onuoha, 2015).

Concerns regarding the uptake of anesthetic agents into breast milk and potential pharmacological side effects passed to the breastfeeding infant influences anesthesia providers' recommendations for the resumption of breastfeeding. Unwarranted fear of lasting sedative effects to the nursing infant and the possibility of delayed brain development has resulted in some anesthesia providers recommending that mothers discard breast milk and delay resumption of breastfeeding for up to 24 hours after anesthesia.

Lack of clarity and inconsistent recommendations place unnecessary stress on this population and are a potential barrier for breastfeeding mothers. Mothers who require anesthesia may abandon nursing based on overly conservative and outdated advice from their anesthesia providers leading to unfortunate outcomes for both mother and baby. For these reasons, this DNP project identified evidenced-based research regarding post-anesthetic advice to be imparted to breastfeeding mothers from their anesthesia providers.

Local Problem

Breastfeeding mothers who required surgery, at a community hospital in Arizona, were not provided consistent, evidence-based recommendations for the resumption of breastfeeding following anesthesia. Often mothers were advised to express their milk by way of a mechanical breast pump and dispose of the milk for the first 24 hours following anesthesia. Current evidence supports that once a mother is awake and alert, she may resume breastfeeding (Cobb et al., 2015). According to the American Academy of Pediatrics (2012), maternal anesthesia is rarely a contraindication to breastfeeding, and that a healthy, term neonate can resume breastfeeding once their mother is awake, alert, and able to hold them. Furthermore, the recommendation to pump and discard breast milk for up to 24 hours after anesthesia is only warranted in the preterm infant or otherwise compromised neonate (American Academy of Pediatrics, 2012).

The Significance of the Project to Anesthesia Providers and Healthcare

Breastfeeding has a profound impact on both mother and child. Evidence confirms that breastfeeding is the healthiest, safest, and best source of infant nutrition (Breastfeeding, 2015). The long-term benefits to the mother after breastfeeding include decreased risk of reproductive cancers, psychological benefits, and optimal metabolic profile. A child who receives breast milk has a reduced risk of atony, obesity, metabolic, and immunologic disorders. Despite the recognized evidence that breastfeeding saves lives and reduces the disease burden for both mother and baby, mothers continue to confront barriers to breastfeeding (Office of the Surgeon General, 2011).

This DNP project intended to present current evidence-based recommendations for the resumption of breastfeeding following anesthesia. To improve the clinical practice for anesthesia

providers counseling breastfeeding mothers, serving to remove barriers to breastfeeding and improve maternal and infant health outcomes.

Purpose

The purpose of this project was to furnish anesthesia providers with current research of anesthetic drugs and their transfer to breast milk. This project aimed to provide evidence-based recommendations to anesthesia providers regarding instructions on breastfeeding after anesthesia. Updating current practice will result in consistent information relayed to the breastfeeding mother, which may help reduce anxiety in this population and ultimately improve satisfaction and outcomes.

THEORETICAL FRAMEWORK

Rogers Diffusion of Innovation Theory of Organizational Change

A theoretical framework guides the researcher on their quest of innovation adoption. Failure of evidence-based research to progress from experimentation to true adoption within an organization is associated with inadequate project planning and training, resistance to change, and lack of support. Rogers' Diffusion of Innovation Theory of Organizational Change provided unity and infrastructure for designing the implementation strategy and served as the conceptual framework for this DNP project. Defining the theory of research and clinical practice strengthens the probability of successful project implementation and adoption (Eldridge, 2013).

There is a positive correlation between the rate of innovation adoption and response of the individuals within the healthcare system (Crowell, 2016). Constructs supplied by Rogers' theory aid in understanding barriers to innovation adoption and strategies to mitigate those barriers. There are negative forces that present barriers to the adoption of change. Individuals

who are resistant to change are laggards, whereas those that are open to innovation are early adopters. Early adopters are opinion leaders, individuals that are highly influential within an organization and can motivate others to adopt new concepts. Rogers' framework explains that innovation diffusion begins with the change agent attempting to influence others to adopt the innovation (Crowell, 2016). This DNP student, as the change agent, fostered an environment of collaboration and openness. The change agent worked within the complex social system, utilizing early adopters to champion innovation diffusion. These early adopters influence the late majority and the lagers, those that are uncomfortable or resistant to change to align (Rogers, 1995). Appreciation and promotion of a social structure that facilitates diffusion is essential for successful project adoption. Rogers's theory helped in the identification of those individuals that supported the project momentum and aided in the adoption of new practice recommendations for the resumption of breastfeeding after anesthesia.

Concepts

A professor of communication, Everett Rogers, theorized on the rate of adoption by individuals within an organization when faced with change or innovation (Melnyk & Fineout-Overholt, 2011). The five main constructs of Rogers's Diffusion of Innovation Model describe the process by which innovation flows through a social system network over time and leads to adoption (Figure 1).

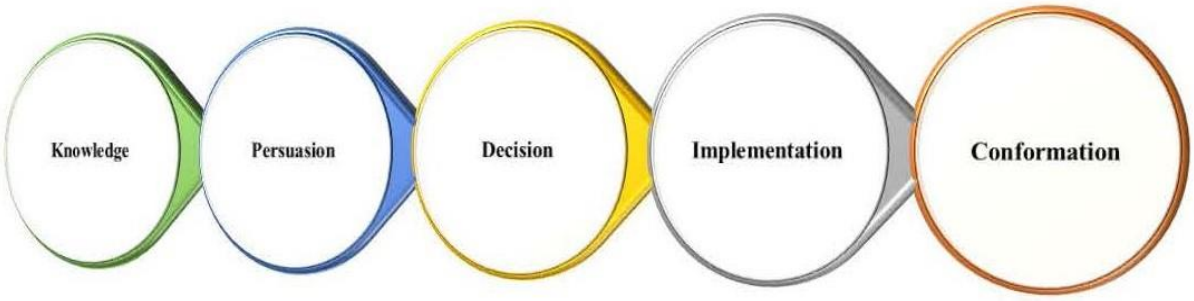


FIGURE 1. Stages of innovation adoption. (Modified from Crowell, D. M. (2016). *Complexity leadership: Nursing's role in health care delivery (2nd ed.).* Philadelphia, PA: F.A. Davis Company.)

Knowledge. The knowledge stage is the creation of awareness. The anesthesia provider gained an understanding of current evidence-based recommendations for the resumption of breastfeeding after anesthesia. The spread of knowledge results in improved patient satisfaction and health outcomes for both mother and baby.

Persuasion. Persuasion is the stage where the anesthesia provider accepts current evidence-based recommendations for the resumption of breastfeeding. Providing anesthesia providers with current evidence of anesthetic drugs and their transfer to breast milk satisfies the need for knowledge with the ultimate goal to shape attitudes and the advice provided to breastfeeding patients.

Decision. The decision stage manifests as the anesthesia provider forming an attitude toward the current evidence and the decision to accept the recommendations. Failure to adopt current recommendations is mitigated by strategic planning and compressive training that aims to demonstrate the vital impact of consistent information relayed to the breastfeeding mother which overall may help reduce anxiety in this population.

Implementation. Implementation is the stage where the anesthesia provider begins to supply their breastfeeding mothers with consistent, evidence-based recommendations for the

resumption of breastfeeding. During this stage, the anesthesia provider will determine if these recommendations are helpful to their patients and if they warrant current use.

Conformation. Both the individual anesthesia provider and the group of anesthesia providers as a whole choosing to adopt and utilize the recommendations when advising their patients on to the resumption of breastfeeding after anesthesia mark confirmation.

SYNTHESIS OF EVIDENCE

A literature review identified current evidence in regards to anesthetic drug diffusion into breast milk and recommendations for breastfeeding mothers who require anesthesia. The following online literature archives were utilized; PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHAL), and Excerpta Medical dataBASE (EMBASE). Key terms used for the search included *breastfeeding, and general anesthesia, anesthetic agents, analgesic agents, infant drug exposure, breast milk transfer,* and *medication.* Additional inclusion criteria included articles published after 2013; English language, human subjects, and randomized clinical research studies. The outcome was 15 articles, with all studies focused on labor-related analgesia and anesthesia. Broadening inclusion criteria to articles published in the last ten years and non-randomized clinical research resulted in 33 articles.

Ethical constraints and difficulty recruiting nursing mothers and infants for controlled studies limit current research information. A large portion of literature about this topic did not qualify for inclusion based on publishing dates greater than 10 years. The peer-reviewed database LactMed®, provided by the National Institute of Health (NIH), was employed for the additional literature search. The database provides a synthesis of validated scientific literature regarding drugs and other chemicals to which breastfeeding mothers may be exposed to, levels

of such substances found in breast milk after maternal administration, and possible adverse effects in the nursing infant (LactMed®, 2017).

Critical appraisal of evidence is necessary to ascertain the strength and weakness of current research and determine transferability into clinical practice. Ten articles (Appendix E) from the literature search met the rigor of this review, based on their relevancy, validity, and reliability.

Strengths

A seven-level hierarchy presented by Polit and Beck (2012) was utilized to assign a level of evidence based on the strength and quality of evidence provided. Evidence retrieved included one randomized control trial (Level II), cohort studies and non-randomized control trials (Level III), and observational and case studies (Level IV). Levels of evidence, based on the source of evidence was fair concerning a lack of randomized control trials related to a preponderance of benefit over harm.

There is objective evidence and extensive research concerning drug chemistry and factors that influence maternal drug transfer into breast milk and subsequent infant exposure to said drugs. The overwhelming evidence suggests that drugs administered to a breastfeeding mother during the perioperative period will not precipitate adverse outcomes in the healthy breastfed infant (Dalal, Bosak, & Berlin, 2014). A breastfeeding mothers' return to baseline mentation and strength suggests drug redistribution from plasma and milk, and termination of drug action (Cobb et al., 2015). Furthermore, there is no required waiting period or discarding of milk necessary before the resumption of breastfeeding once a mother has recovered from general anesthesia (Chu et al., 2013; Dalal et al., 2014; Kelly et al., 2012; Shergill et al., 2012). In most

cases, general anesthesia is administered for a short period utilizing a combination of anesthetic agents. When delivering a combination of anesthetic agents, several authors suggest to adhere to the recommendations for the most problematic medication used during the procedure; caution is advised for anesthetic agents with prolonged half-lives and potent metabolites that may lead to drug accumulation (LactMed®, 2017; Sachs, 2013; Shergill et al., 2012). The American Academy of Pediatrics Committee on Drugs surmises, "*The benefits of breastfeeding outweigh the risk of exposure of most therapeutic agents via breastmilk*" (Sachs, 2013, p. 805).

Weaknesses

Weaknesses identified in the literature include a limited pool of current high-level research studies, finding that most notable and established studies concerning breastfeeding and anesthetic agents were published over a decade earlier. Due to ethical constraints and the considerably small population of breastfeeding mothers who require general anesthesia, there is a scarcity of large or robust studies in this population. Current scientific literature is limited to observational studies, retrospective cohort studies, case studies, and literature reviews focusing on pharmacological properties of anesthetic agents (Dalal et al., 2014; Kelly et al., 2012; Nitsun et al., 2006; Shergill et al., 2012). Lack of robust studies with randomization, small sample size, and limited sample settings that predominate current literature challenges credibility and can undermine transferability of current literature. Additionally, gaps identified include lack of human data, specifically studies that detect the presence of many commonly used anesthetic agents in breast milk (e.g., ketamine, sevoflurane, remifentanil). Not found in the literature are studies that evaluate the transfer of drugs via breast milk to children that may reveal different pharmacodynamic profiles since there is an increased amount of breast milk consumption and

therefore drug ingestion in this population (Chu et al., 2013). Due to the fragility of premature and special needs infants, there is limited information in regards to recommendations for resumption of breastfeeding in this distinctive population.

Current Literature

The mechanism of transfer of most commonly used anesthetic drugs into breast milk is by passive diffusion and based on the physiochemical properties of the anesthetic agent. Those drugs that are highly protein bound, less lipid soluble, have a lower pKa and a larger molecular weight lack the ability to penetrate breast milk (Dalal et al., 2014). Drugs used during the perioperative period are classified into standard pharmacological categories of analgesic opioids, benzodiazepines, intravenous anesthetic agents, local anesthetics, neuromuscular blockers and reversal agents, volatile anesthetics, and antiemetics.

Analgesic Opioids

Judicious administration of analgesic opioids in the perioperative period is a requisite for anesthetic practice due to their risk of maternal and infant respiratory depression, hypercapnia, and hypoxemia. Discussion of commonly used opioids, their transfer into breast milk, and recommendations are below.

Fentanyl. Favored for its short duration of action and fast onset, Fentanyl is one of the most commonly administered opioids utilized for analgesia during the perioperative period. Authors established that maternal administration of fentanyl in the perioperative period was unlikely to result in adverse outcomes for a healthy, term breastfeeding infant; there is no requirement for milk discarding or waiting for the resumption of breastfeeding (Nitsun et al., 2006; Shergill et al., 2012).

Remifentanil. Remifentanil may be a promising perioperative opioid analgesic for breastfeeding mothers due to its unique pathway of metabolism in the serum, rapid onset and offset, lack of accumulation and rapid recovery after discontinuation (Flood et al., 2015). Four case studies presented by Stuttmann, Schafer, and Hilbert (2010) reported no adverse outcomes or signs of sedation in breastfed infants after maternal administration of remifentanil as part of their general anesthetic. However, remifentanil is an unsuitable option for the treatment of acute postoperative pain due to its brief context-sensitive half-life of less than 10 minutes.

Morphine. Considered less potent when compared to fentanyl, morphine is a commonly used opioid in anesthetic practice favored for its longer duration of action and treatment of postoperative pain, reaching peak effect 90 minutes after intravenous administration (Flood et al., 2015). However, morphine is associated with a greater depression of ventilatory response to hypoxia in women. Metabolized to an active, more potent metabolite morphine-6-glucurcoids requires renal elimination (Flood et al., 2015). Morphine secretion in breast milk was studied in the literature over two decades ago. Earlier studies suggest that the amount of maternally transferred morphine to the breastfeeding infant is variable and warrants caution (Robieux et al., 1990; Baka et al., 2002). Furthermore, infants under one month of age, exposed to morphine are at an increased risk of sedation and respiratory problems due to immature metabolization and clearance of the drug (Hale, 2017). The evidence suggests extreme caution or avoidance of morphine administration to the breastfeeding mother (Dalal et al., 2014).

Other. Current literature suggests that perioperative administration of other analgesic opioids such as meperidine and hydromorphone are not agents of choice in lactating women as

there is an increased risk of respiratory depression for the breastfeeding infant (Dalal et al., 2014).

Benzodiazepines

Midazolam is one of the most common benzodiazepines administered as part of a general anesthetic for its sedating and anxiolytic effects. Several authors suggest that midazolam, administered perioperatively, was not likely to affect a healthy, term infant, which supports the resumption of breastfeeding after surgery (Nitsun et al. 2006; Dalal et al. 2014). The use of perioperative diazepam or lorazepam is unsafe for the breastfeeding infant and should be avoided.

Intravenous Anesthetic Agents

General anesthesia requires the administration of intravenous anesthetic agents, which cause a reversible loss of consciousness. Commonly used intravenous anesthetic agents include propofol, ketamine, and etomidate. Due to their short duration of action and rapid metabolism with no active metabolite, propofol and etomidate are safe for administration in the breastfeeding mother with no waiting period necessary for the resumption of breastfeeding (Cobb et al., 2015). The combined administration of ketamine and propofol decreases postoperative pain and opioid consumption in breastfeeding mothers (Jaafarpour, Vasigh, Khajavikhan, & Khani, 2017). Research in the literature regarding maternal administration of ketamine and the subsequent exposure to the breastfeeding infant is nonexistent. Ketamine's known short half-life, and rapid redistribution out of plasma suggests milk levels of ketamine would be low after maternal administration (Hale, 2017; LactMed®, 2017). Current recommendations for ketamine

administration in the breastfeeding mother are for the close monitoring of the infant post maternal administration.

Local Anesthetics

Local anesthetics physiochemical properties limit their ability to transfer into breast milk and furthermore are poorly absorbed by the breastfeeding infant (Chu et al., 2013; Cobb et al., 2015). Authors established that intravenous, peripheral, or neuraxial administration of lidocaine results in minimal lidocaine concentrations in breast milk, does not precipitate adverse effects in the nursing infant, and decreases postoperative opioid requirements for nursing mothers (Chu et al., 2013; Cobb et al., 2015; Thawart et al., 2016). Neuraxial administration of lidocaine, bupivacaine, or ropivacaine is safe to use in lactating women, and no special precautions are required (Cobb et al., 2015; Dala et al., 2013).

Neuromuscular Blockers and Reversal Agents

General anesthesia often requires neuromuscular relaxation to facilitate ease of endotracheal intubation and a favorable surgical environment. Chemical properties inherent to neuromuscular blocking agents including, large molecular size, poor lipid solubility, and polarized nature, restrict their ability to diffuse into breast milk passively and are presumed safe for use in lactating women (Dala et al., 2014; Chu et al., 2013; Cobb et al., 2015). Besides, the rapid metabolization and poor oral bioavailability of commonly used neuromuscular blocking agents, succinylcholine, vecuronium, rocuronium, and cisatracurium, demonstrates the unlikelihood of these agents to reach breast milk in sufficient concentrations or reach the bloodstream of a breastfeeding infant (Dala et al., 2014). The combination of an acetylcholinesterase-inhibiting agent (neostigmine) and an anticholinergic agent (glycopyrrolate)

is administered to reverse neuromuscular relaxation. As quaternary ammonium compounds, the physiochemical properties of neostigmine and glycopyrrolate prevent their ability to penetrate the blood-milk barrier easily and are unlikely to affect the breastfed infant (Dala et al., 2014; Cobb et al., 2015; LactMed®, 2017).

Inhaled Anesthetics

There is no published data in regards to inhaled anesthetic levels measured in human milk. Inhaled anesthetics have poor bioavailability, rapidly eliminated once administration ceases via alveolar ventilation (Flood et al., 2015). Based on the available evidence and known pharmacokinetics of the elimination of inhaled anesthetics, absorption by the breastfeeding infant is likely nil and no discarding of milk or waiting period is required (Bhaskara et al., 2016; Dala et al., 2014; Reece-Stremtan, Campos, & Kokajko, 2017).

Antiemetics

Ondansetron and metoclopramide are commonly used agents for the prevention and treatment of postoperative nausea and vomiting. As well, these agents have been administered to lactating women for treatment of nausea after cesarean section (ondansetron) and as galactagogues (metoclopramide) (LactMed®, 2017). Ondansetron and metoclopramide readily cross the blood-milk barrier; however, no adverse infant effects have been reported and may be safely used in lactating women (Dala et al., 2014; Chu et al., 2013; Elkomy et al., 2015).

ETHICAL CONSIDERATIONS

Institutional Review Board (IRB) approval from the facility this project was implemented was obtained before implementation in the clinical setting. With the intent to demonstrate respect for all participants, the purpose of this project was explained and full disclosure of all parts of

this DNP project made available. Participant's anonymity and confidentiality was maintained through utilization of the My AGREE PLUS platform. Explanation of the risks and benefits provided, emphasizing that, study outcomes would not result in judgment, criticism, or misuse (Polit & Beck, 2012). Described as a moral obligation to act in kindness and do well, the principal beneficence was demonstrated by treating all participants with kindness and respect. Project transparency in regards to project purpose and potential implications for future research was disclosed. All participants were treated judiciously, with no distinction made between participants based on personal characteristics, experience, competence, or merit. With the intent to demonstrate fairness and equality, all participants were given the opportunity to complete the same questionnaire; no questions were altered at any time. The project leader honored all agreements made with participants, respecting their personal choice to participate or not participate in this DNP project.

METHODS

Project Design

Rogers' Diffusion of Innovation Theory of Organizational Change was instrumental as a guide for this DNP project. The first two stages of organizational change were implemented with the development of a CPG and the dissemination of the evidence to key stakeholders.

The working framework utilized for this DNP project was the Appraisal of Guidelines for Research and Evaluation (AGREE II) Instrument. The AGREE II provides a systematic strategy for the development of guidelines and serves as a tool to assess the quality, rigor, and transparency of the developed guideline. The AGREE II framework is a validated tool that meets all criteria outlined by the Institute of Medicine for the development and assessment of CPGs.

The first phase of this DNP project involved the systematic development of a CPG based on current evidence in the literature. Methods used for collection and selection of current evidence was previously discussed in this paper. The development of an evidence-based clinical guideline requires the author to identify and weigh the quality and strength of the evidence to support the recommendations. Levels of evidence supporting recommendations were based on the National Guideline Clearing House (Figure 2).

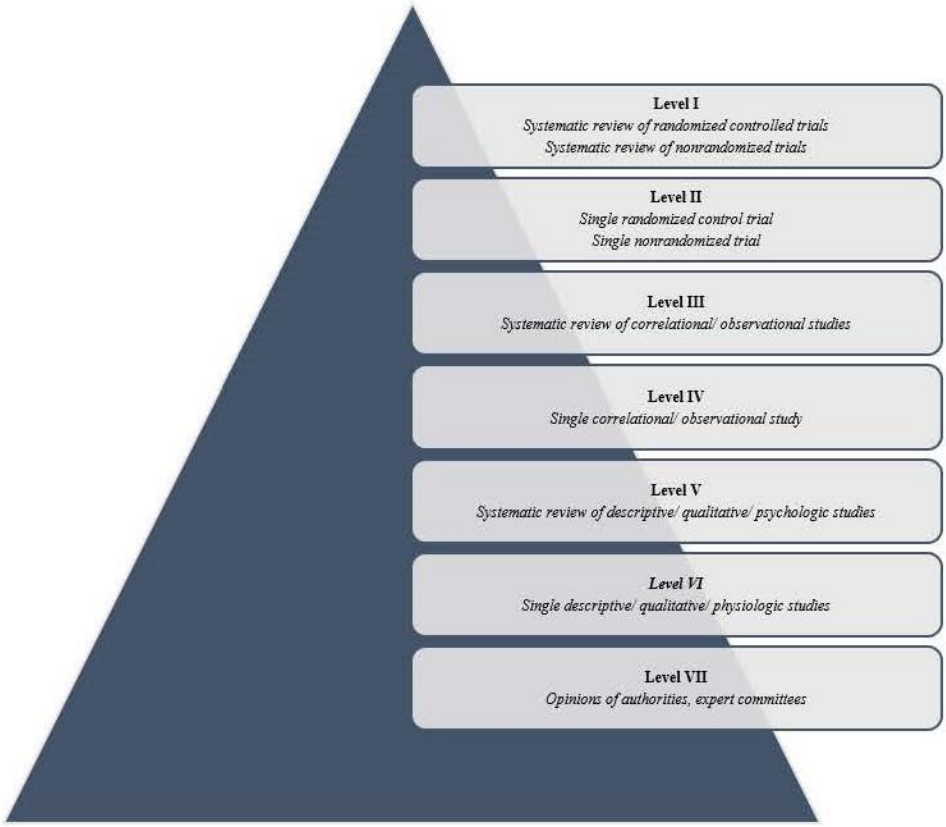


FIGURE 2. Evidence hierarchy of designs. (Based on the National Guideline Clearing House adapted from Polit, D. F. & Beck, C. T. (2012). *Nursing research. Generating and assessing evidence for nursing practice (9th ed.).* Philadelphia, PA: Wolters Kluwer; Lippincott, Williams & Wilkins.)

The second phase of this DNP project was accomplished by utilizing the Appraisal of Guidelines for Research and Evaluation II (AGREE II) framework. An interdisciplinary panel consisting of a pharmacist, two lactation specialists, and one anesthesia provider appraised the

newly developed CPG utilizing the AGREE II instrument. The AGREE II tool provided a guide for appraisers to assess the quality of the developed guideline via six domains and two global rating items to increase the reliability of the developed CPG.

Setting and Participants

The audience for this DNP project included anesthesia providers (n=11) at a mid-sized rural facility in Northern Arizona for which this CPG was developed. The interdisciplinary panel of critical appraisers (Figure 3) involved in assessing the quality of the CPG included one pharmacist, two lactation specialists, and one anesthesia provider licensed to practice in their respected fields in the state of Arizona. A multidisciplinary panel consisting of greater than four appraisers increases the reliability of the developed CPG assessment (Brouwers et al., 2010).

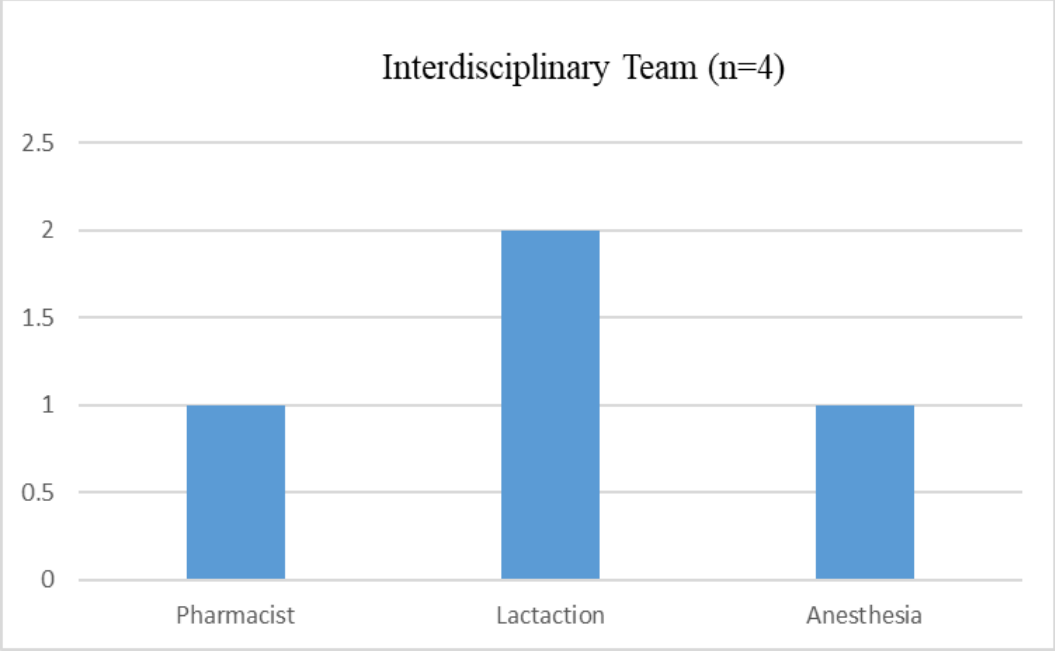


FIGURE 3. Critical appraisers.

Data Collection

Project data collection for the second phase of this project began after organizational and IRB of Northern Arizona University approval. The My AGREE PLUS platform was utilized to evaluate and assess the developed CPG by the interdisciplinary panel. The My AGREE PLUS platform is a free, online, electronic platform that allows appraisers to collaborate and evaluate a particular practice guideline using the AGREE II assessment tool (Brouwers et al., 2010). The AGREE II assessment tool (Appendix C) is comprised of 23 key items organized within six domains and two overall guideline assessments. These six domains: 1) scope and purpose; 2) stakeholder involvement; 3) rigor of development; 4) clarity of presentation; 5) applicability; and, 6) editorial independence assess the overall quality of the guidelines and its recommendation into practice (AGREE Next Steps Consortium, 2017). The two global guideline assessments: 1) rate the overall quality of this guideline, and 2) I would recommend this guideline for use required the AGREE II evaluator to determine if this CPG was a quality guideline to be implemented (AGREE Next Steps Consortium, 2017).

Each AGREE II key items are rated on a Likert seven-point scale, from ‘1’ point representing *strongly disagree* to ‘7’ points representing *strongly agree*. The summated rating scale uniquely captures the dimensions of the developed CPG and shows clear discrimination of the guideline quality (AGREE Next Steps Consortium, 2017).

To promote standardization of scoring, each panel member was required to sign a written statement (Appendix C) that confirms his or her completion of a brief online tutorial for the AGREE II assessment tool before assessment of the developed CPG. A welcome packet was provided for all appraisers that included; a welcome letter introducing the DNP project

(Appendix A), instructions on how to complete the online AGREE II assessment tutorial, and how to contact the project leader for any questions or concerns related to this DNP project. Appraisers were given a copy of the AGREE II assessment tool (Appendix B) and manual with a three-week window in which to complete the online tutorial and AGREE II assessment of the developed CPG.

Data Analysis

A quality score was calculated for each of the AGREE II six domains independently. The domain scores were calculated by summing up all scores of individual items in each domain and scaling the total as a percentage of the maximum possible score for that domain (AGREE Next Steps Consortium, 2017). A maximum possible score was calculated for each domain [7 (strongly agree) x (domain items) x 4 (number of appraisers)]. Next, a minimum possible score was calculated for each domain [1 (strongly disagree) x (domain items) x 4 (number of appraisers)]. Last, the scaled individual domain scores were calculated [(Obtained score – Minimum possible score) / Maximum possible score – Minimum possible score)] x 100. The final score was reported in a percentage for each domain.

RESULTS

The AGREE II online guideline appraisal provided individual scores for all 23 questions along with the opportunity for appraisers to add personal comments for all items. A cumulative score for each of the six domains resulted with a final overall guideline assessment rating the quality of the developed guideline. The Seven-Point Agree II Score Calculator and Decision Rules were utilized to calculate the combined score of all appraisers and determine guideline quality. The detailed results of the appraisal can be found in table format (Figure 4). A quality

threshold of all domain scores higher than 80% indicates a high-quality guideline. A quality threshold of greater than 80% was assigned to each domain meaning that no revisions are needed.

The overall quality (OA1) of the developed guideline was assessed and resulted in a combined score of 92%, representative of a high-quality guideline. Demonstrating low discrepancy between appraisers, the standard deviations for all domains were less than 0.5%. The overall combined score of the six domains were 96%, 88%, 89%, 97%, 97%, and 100% (Figure 4) respectively, indicating that no action is necessary to revise the developed CPG. Appraisers overall judgment concerning recommended use of the developed guideline resulted with an answer of 'Yes,' to the recommended use of the guideline.

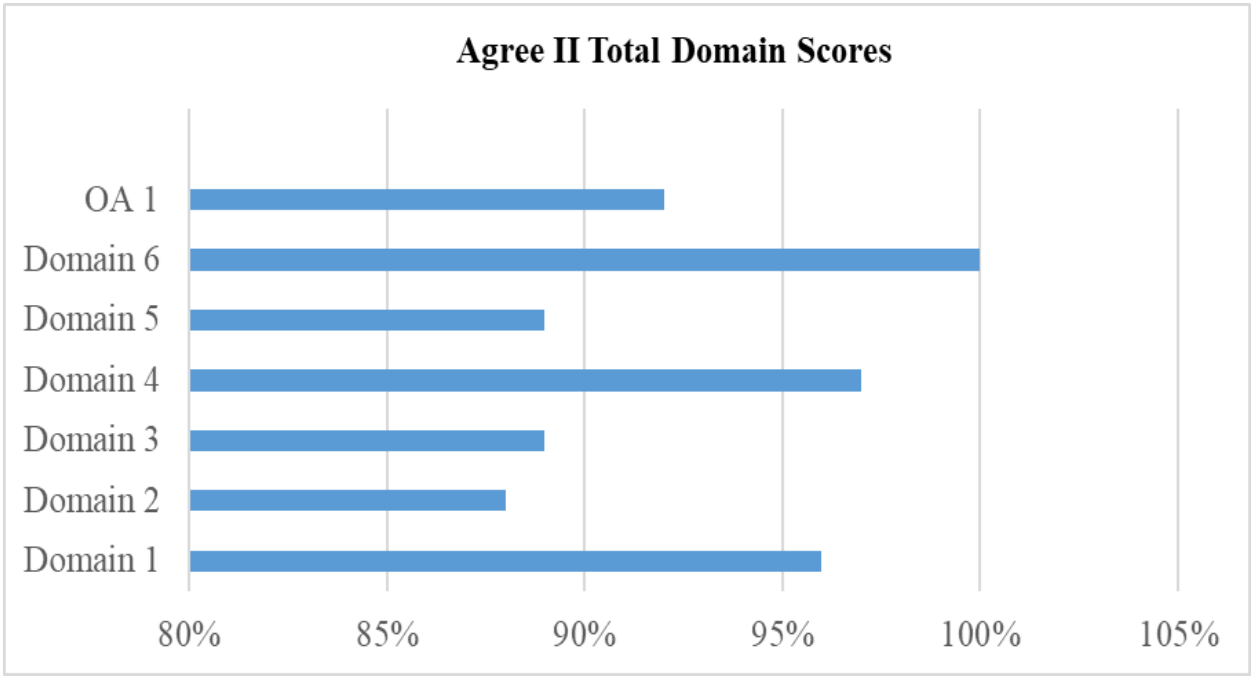


FIGURE 4. Agree II total domain scores. (Greater than 80%=no revisions needed and high-quality guideline. OA1=overall quality.)

Based on the calculated scores and the appraiser's comments, the developed guideline meets the criteria of a high-quality clinical practice guideline. Although no action is required to revise the guideline based on the calculated scores, the opportunity for appraisers to provide individual comments for each of the 23 questions aided in identifying strengths and weakness of the developed CPG. Comments and recommendations given by appraisers are to be addressed, to ensure the quality and ultimate adoption of the developed guideline by stakeholders.

Appraiser Comments

An advantage to the AGREE II online appraisal tool is the ability for appraisers to comment within each domain appraised. Constructive comments to enhance the overall quality of the developed CPG are listed below.

Domain 1

Scope and Purpose Item 2 Appraiser 2: it could have been more advantageous to clearly identify the question.

Domain 2

Stakeholder Involvement Item 4 Appraiser 6: It would have been beneficial to add a Gynecologist within the interdisciplinary team. The guideline should also include the postoperative RN who provides the majority of patient education.

The respondent’s comments enable the project leader to see clear discrimination of appraiser’s views and concerns regarding the developed CPG. Ensuring clear identification of the health question will provide ease of understanding and clarity for users of the developed CPG and serve to increase usability. Including postoperative registered nurses as well as women’s

health providers in the interdisciplinary team aids in validating transferability and adoption of the developed CPG.

DISCUSSION

Strengths

The ability for appraisers to score each domain nominally as well as to add free text comments provided valuable information and insight on the quality of the CPG. An interdisciplinary appraisal team of greater than four member's increases CPG transferability and reliability of data collected. The CPG was developed to reduce the ambiguity of advice imparted to breastfeeding mothers who require general anesthesia. To promote the relay of consistent, current evidence-based information to the breastfeeding mother serves to reduce anxiety in this population and improve outcomes. This DNP project addresses the identified gap in clinical practice and provides a systematically developed high-quality guideline to assist anesthesia providers and their patients about appropriate decisions in regards to the resumption of breastfeeding after general anesthesia.

Limitations

The body of evidence presented in this CPG was accumulated, appraised, and developed into a clinical practice guideline by one person for the purpose of a DNP project. In the setting of DNP scholarly work, the AGREE II tool was utilized as a framework in which to evaluate the developed DNP academic work. The AGREE II tool does not allow for an appraiser to choose a "*Not Applicable*" response in the setting of an AGREE II item that may not be applicable. This may be reflected in the score for Domain 2 Stakeholder involvement, which received a score of

89%. In Domain 2, appraisers were asked to evaluate the stakeholder involvement in the development of the CPG which was not applicable in this setting.

Interpretation of CPG quality based on domain scores is ambiguous, as there is no empirical data to link specific quality scores with implementation outcomes (Brouwers et al., 2010). An approach to aid in the interpretation of domain scores is to assign quality thresholds before beginning the AGREE II appraisal.

Recommendations for Practice

There is objective evidence and extensive research concerning drug chemistry and factors that influence maternal drug transfer into breastmilk and subsequent infant exposure to said drugs. The mechanism of transfer of most commonly used anesthetic drugs into breastmilk is by passive diffusion and based on the physiochemical properties of the anesthetic agent. Those drugs that are highly protein bound, less lipid soluble, have a lower pKa and a larger molecular weight lack the ability to penetrate breastmilk (Dalal et al., 2014). The overwhelming evidence suggests that drugs administered to a breastfeeding mother during the perioperative period will not precipitate adverse outcomes in the healthy breastfed infants (Dalal, Bosak, & Berlin, 2014).

A breastfeeding mothers return to baseline mentation and strength, suggest drug redistribution from plasma and milk, and termination of drug action (Cobb et al., 2015). Furthermore, there is no required waiting period or discarding of milk necessary before the resumption of breastfeeding once a mother has recovered from general anesthesia (Chu et al., 2013; Dalal et al. 2014; Kelly et al., 2012; Shergill et al., 2012). In most cases, general anesthesia is administered for a short period utilizing a combination of anesthetic agents. Several authors suggest that, in general, when administering a combination of anesthetic agents, follow the

recommendations for the most problematic medication used during the procedure and caution is advised for anesthetic agents with prolonged half-lives and potent metabolites that may lead to drug accumulation (LactMed®, 2017; Sachs, 2013; Shergill et al., 2012).

Dissemination of this project was accomplished via an electronic presentation at an anesthesia staff meeting at the Northern Arizona facility. Presently, there is no published CPG that addresses resumption of breastfeeding after general anesthesia. This scholarly DNP project aimed to open the discussion and provide education to anesthesia providers concerning breastfeeding and general anesthesia to aid in the relay of current and evidence-based advice for when to resume breastfeeding after general anesthesia.

The adoption of the developed CPG resulted in positive patient outcomes and decrease ambiguity in advice provided to breastfeeding mothers who require general anesthesia. It served to enhance the anesthesia provider's perioperative management plan and promoted an appropriate and safe post-operative patient care plan.

Adoption of this CPG should be evaluated via a focus group assessment during the first three months of implementation to determine if anesthesia providers are utilizing the developed CPG and identify barriers to adoption if they arise. A procedure for monitoring and updating the guideline should be planned to ensure that the guideline is updated with current evidence when applicable. A CPG is only sustainable if there is a continual study of evolving evidence and modernization of recommendations based on arising evidence.

The Dissemination Plan

Essential to sustainable practice change and the development of future practice, scholarship is the dissemination of knowledge gained in this DNP project. Upon completion of

this DNP project, findings were shared with the Northern Arizona facility during a scheduled meeting for anesthesia providers. The project leader presented the project in a digital PowerPoint presentation with handouts engaging key stakeholders. The presentation was followed by an open discussion where audience members commented that the developed CPG filled a gap in clinical practice. The presentation and developed CPG was praised and accepted for facility adoption. At follow-up evaluation, the Chief of Anesthesia stated: “since the presentation, we have had several breastfeeding mothers, and all anesthesia providers have adopted the new guideline.” This project will also be disseminated at the Arizona Association of Nurse Anesthetists 2019 Fun and Sun Conference and the New Mexico Association of Nurse Anesthetist Nurse Anesthesia Conference 2019.

DNP ESSENTIALS

This DNP project incorporated two significant elements of the DNP Essentials.

DNP Essential III

Clinical Scholarship and Analytical Methods for Evidence-Based Practice. Integration of knowledge from diverse sources across disciplines for the improvement of health outcomes is demonstrated in this scholarly project and fulfills this essential. Critically appraising the existing evidence and facilitating its translation into clinical practice as evidenced by the synthesis of evidence validates competency of this essential.

DNP Essential VI

Interprofessional Collaboration for Improving Patient and Population Outcomes is represented in this project through the facilitation of an effective interprofessional team and demonstrates this project leader's ability to be an effective team leader.

CONCLUSION

The developed CPG provides anesthesia providers with a synthesis of research findings and strong, evidence-based recommendations regarding the resumption of breastfeeding after general anesthesia. Translation of research into clinical practice remains to be a challenge in healthcare; however, the developed CPG serves to bridge the gap between research and clinical practice to improve patient outcomes in this unique population. Future implications include dissemination of the developed CPG to ancillary staff including registered nurses and lactation specialists that work closely with breastfeeding mothers. To continue to improve and strengthen the CPG, women's health care providers; obstetrician, midwives, and gynecologists, as well as registered nurses, should be a part of the interdisciplinary team.

APPENDIX A:

PARTICIPANT WELCOME LETTER

Dear Provider,

My name is Lacey Gibson, and I am a nurse currently perusing my doctorate in Nurse Anesthesia at the University Of Arizona. I am writing to invite you to participate in my DNP project about breastfeeding after anesthesia. The purpose of this DNP project is to develop a clinical practice guideline (CPG) for the resumption of breastfeeding after general anesthesia. You are being asked to participate in this project because you currently work in a relevant health profession and are considered a key stakeholder for the planned, developed clinical practice guideline.

Participation in the study entails completing the AGREE II Overview Tutorial which can be found at http://www.agreetrust.org/resource-centre/agree-ii-training-tools// and then appraising the developed CPG utilizing the AGREE II assessment tool. An email will be sent directly from the My AGREE Plus platform with directions and links to complete the online CPG appraisal.

Completing the online CPG appraisal and participating in this project is entirely voluntary, and implies informed consent. If you decide to participate in this study, all data collected will remain confidential and anonymous. Information gathered through this project will be used for this DNP project and may be used for the development of future scholarly projects. At this time, the author has no plans to publish the information gathered from this study. This study was reviewed and found to be acceptable by the Institutional Review Board responsible for human subjects at Northern Arizona University, which serves to protect the rights and welfare of participants in research under university policies, state, and federal regulations. Participation in the study does not revoke the legal right you have as a participant.

Your choice to participate in this study is entirely voluntary with no known risks. You may choose to decline or stop participation at any time during the study. Your decision to refuse or stop participation will be respected and will not affect any future relationship with the University of Arizona or affiliated organization.

For questions, concerns, or complaints related to this study, please feel free to contact the researcher, Lacey Gibson at laceygibson@email.arizona.edu or (602) 315-8661. As well, if you have questions or concerns regarding your rights as a participant in this study or to discuss study-related concerns you are encouraged to contact the Human Subjects Protection Program at your facility.

Thank you for your time and consideration in supporting my DNP project.

Lacey Gibson, BSN, RN, SRNA-DNP
laceygibson@email.arizona.edu
(602) 315-8661

APPENDIX B:

AGREE II ASSESSMENT TOOL

AGREE II ASSESSMENT TOOL

Domain 1. Scope and Purpose		**1 SD**	**2**	**3**	**4**	**5**	**6**	**7 SA**
1	The overall objective (s) of the guideline is (are) specifically described.							
2	The health question (s) covered by the guideline is (are) specifically described.							
3	The population to whom the guideline is meant to apply is specifically described.							
Domain 2. Stakeholder Involvement		**1 SD**	**2**	**3**	**4**	**5**	**6**	**7 SA**
4	The guideline development group includes individuals from all relevant professional groups.							
5	The views and preferences of the target population have been sought.							
6	The target users of the guideline are clearly defined.							
Domain 3. Rigor of Development		**1 SD**	**2**	**3**	**4**	**5**	**6**	**7 SA**
7	Systematic methods were used to search for evidence.							
8	The criteria for selecting the evidence are clearly described.							
9	The strengths and limitations of the body of evidence are clearly described.							
10	The methods for formulating the recommendations are clearly described.							
11	The health benefits, side effects, and risks have been considered in formulating the recommendations.							
12	There is an explicit link between the recommendations and the supporting evidence.							
13	The guideline has been externally reviewed by experts before its publication.							
14	A procedure for updating the guideline is provided.							
Domain. Clarity of Presentation		**1 SD**	**2**	**3**	**4**	**5**	**6**	**7 SA**
15	The recommendations are specific and unambiguous.							
16	The different options for management of the condition or health issue are clearly presented.							
17	Key recommendations are easily identifiable.							
Domain 5. Applicability		**1 SD**	**2**	**3**	**4**	**5**	**6**	**7 SA**
18	The guideline describes facilitators and barriers to its application.							
19	The guideline provides advice and/or tools on how the recommendations can be put into practice.							
20	The potential resource implications of applying the recommendations have been considered.							

21	The guideline presents monitoring and/ or auditing criteria.							
Domain 6. Editorial Independence		**1 SD**	**2**	**3**	**4**	**5**	**6**	**7 SA**
22	The views of the funding body have not influenced the content of the guideline.							
23	Competing interests of guideline development group's members have been recorded and addressed.							

SD (strongly disagree) **SA** (strongly agree)

Overall Guideline Assessment
For each question, please choose the response which best characterized the guideline assessed

		1 Lowest quality	**2**	**3**	**4**	**5**	**6**	**7 Highest quality**
1	Rate the overall quality of this guideline							
		YES		YES, with modifications			NO	
2	I would recommend this guideline for use							

APPENDIX C:

AGREE II TUTORIAL COMPLETION AFFIDAVIT

This letter serves to confirm that I, _____

have been provided a copy of the AGREE II assessment tool and user manual. That I have completed the AGREE II assessment tool online tutorial and been provided access to the AGREE II practice exercise in preparation for completing a formal appraisal of the developed Clinical Practice Guideline for Breastfeeding after Anesthesia.

_____

Signature Date

APPENDIX D:

CLINICAL PRACTICE GUIDELINE:

BREASTFEEDING AFTER GENERAL ANESTHESIA

Clinical Practice Guideline: breastfeeding after general anesthesia

Introduction

Inconsistent and often conflicting post-anesthetic advice imparted to breastfeeding mothers leads to unnecessary weaning or premature abandonment of nursing. The advice in regards to the resumption of breastfeeding and milk discards vary depending on anesthesia provider opinion, medical facility protocol, or the favored medically endorsed guideline. Furthermore, anesthesia providers, hospitals, and patients may rely on conservative and often restrictive recommendations given by drug manufacturers that do not accurately reflect conditions for lactating women and the transfer of anesthesia and analgesia medications into breast milk (Cobb, Liu, Valentine, & Onuoha, 2015).

Lack of clarity and inconsistent recommendations places unnecessary stress on this population and is a barrier for breastfeeding mothers. Mothers who require anesthesia may abandon nursing based on overly conservative and outdated advice from their anesthesia providers leading to unfortunate outcomes for both mother and baby. For these reasons, this CPG sets out to identify evidenced-based research regarding post-anesthetic advice to be imparted to breastfeeding mothers.

Scope and purpose

Guideline objective

This CPG intends to furnish breastfeeding mothers and their anesthesia providers with evidence-based recommendations for the resumption of breastfeeding after general anesthesia. Updating current practice will result in consistent information relayed to the breastfeeding mother, serving to remove a barrier to breastfeeding and improve maternal and infant health outcomes.

Target population

Breastfeeding mothers who require anesthesia, breastfeeding infants.

Note: This guideline is a clinical guideline for the resumption of breastfeeding after general anesthesia, outside the postpartum period.

Stakeholder involvement

The guideline was developed by an interdisciplinary team consisting of stakeholders that represent the intended users of the guideline, anesthesia provider, lactation consultant, and pharmacist.

Mythology

Methods used to collect/ select evidence

A search of electronic databases

Description of Methods Used

A literature review was undertaken to identify current evidence in regards to anesthetic drug transfer via breastmilk and recommendations for breastfeeding mothers who require anesthesia. The following online literature archive databases were used, PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHAL), and Excerpta Medical database (EMBASE). Key terms used in the search included breastfeeding, general anesthesia, anesthetic agents, analgesic agents, infant drug exposure, breastmilk transfer, and medication. Additional inclusion criteria included articles published after 2013; English language, human subjects, and randomized clinical research studies. The outcome was fifteen articles, with all studies focused on labor-related analgesia and anesthesia. Broadening inclusion criteria to articles published in the last ten years and non-randomized clinical research resulted in thirty-three articles.

Ethical constraints and difficulty recruiting nursing mothers and infants for controlled studies limit current research information. A large portion of literature about this topic did not qualify for inclusion based on publishing dates greater than ten years. Therefore, a literature search for commonly used anesthetic drugs and their transfer into breastmilk was conducted. The peer-reviewed database provided by the National Institute of Health (NIH) LactMed® was utilized for the additional literature search. Drugs and other chemicals to which breastfeeding mothers may be exposed to, as well as levels of such substances found in breastmilk and possible adverse effects in the nursing infant, is reviewed from scientific literature, validated, and provided by LactMed®. (LactMed®, 2017).

Number of Source Documents

Ten articles from the literature met the rigor of this review, based on their relevancy, validity, and reliability. All articles were published after 2012.

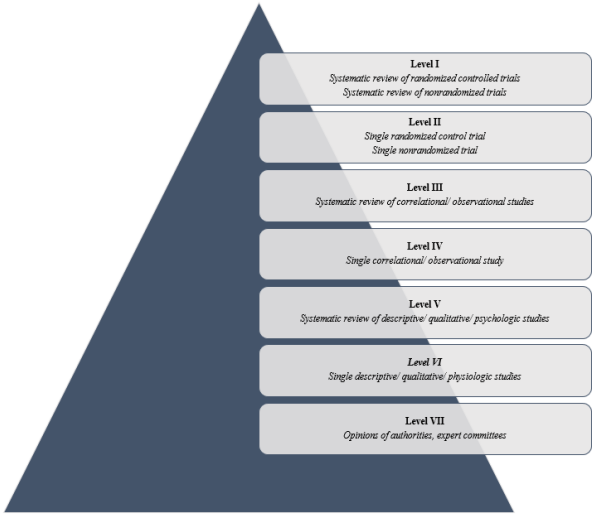
Methods used to assess the quality and strength of evidence.

A 7-level hierarchy presented by Polit & Beck was utilized to assign a level of evidence based on the strength and quality of evidence provided (2012). The grade of recommendation was assigned utilizing Strength of Recommendation Taxonomy (SORT) developed by the editors of the U.S. family of medicine and primary care journals (Ebell et al., 2004).

The use of two rating scales accommodates for the strength of evidence based on evidence source and the context of the clinical practice setting that the recommendation will be applied (Dicenso et al., 2005). Evidence retrieved included one randomized control trial (Level IIa), cohort studies and non-randomized control trials (Level IIIa), and observational and case studies (Level IVa). Levels of evidence, based on the source of evidence, was fair in respect to a lack of randomized control trials related to a preponderance of benefit over harm.

Rating scheme for the strength of evidence

Level of Evidence



Strength of Evidence

Grade of Recommendation	*Definition*
A	Recommendation based on consistent and good quality of patient orientated evidence. Well designed randomized control trials or overwhelming consistent evidence from observational studies performed on a population similar to the guideline's target population.
B	Recommendation based on inconsistent or limited quality of evidence, observational studies (case control and cohort design) with minor limitations.
C	Recommendations based on consensus, usual practice, expert opinion, disease-oriented evidence, or case series for studies of prevention, screening, diagnosis, or treatment.

Description of Methods of Guideline Validation

The final draft of the developed CPG underwent extensive external review by an interdisciplinary panel representing the specialties of anesthesia, pharmacy, and lactation. The My AGREE PLUS platform was utilized which provides a summated rating score that uniquely captures dimensions of the developed CPG and shows clear discrimination of the guideline quality.

Recommendations

General statement

There is objective evidence and extensive research concerning drug chemistry and factors that influence maternal drug transfer into breastmilk and subsequent infant exposure to said drugs. The overwhelming evidence suggests that drugs administered to a breastfeeding mother during the perioperative period will not precipitate adverse outcomes in the healthy

breastfed infants (Dalal, P., Bosak, J. & Berlin, C., 2014). A breastfeeding mothers return to baseline mentation and strength, suggest drug redistribution from plasma and milk, and termination of drug action (Cobb et al., 2015). Furthermore, there is no required waiting period or discarding of milk necessary before the resumption of breastfeeding once a mother has recovered from general anesthesia (Chu et al., 2013, Dalal et al. 2014, Kelly et al., 2012, Shergill et al., 2012). In most cases, general anesthesia is administered for a short period utilizing a combination of anesthetic agents. Several authors suggest that, in general, when administering a combination of anesthetic agents, follow the recommendations for the most problematic medication used during the procedure and caution is advised for anesthetic agents with prolonged half-lives and potent metabolites that may lead to drug accumulation (LactMed®, 2017, Sachs, 2013, Shergill et al., 2012).

The American Academy of Pediatrics Committee on Drugs surmises, "The benefits of breastfeeding outweigh the risk of exposure of most therapeutic agents via breastmilk" (Sachs, 2013, p. 805).

Standard anesthetic agents and Recommendations

The mechanism of transfer of most commonly used anesthetic drugs into breastmilk is by passive diffusion and based on the physiochemical properties of the anesthetic agent. Those drugs that are highly protein bound, less lipid soluble, have a lower pKa and a larger molecular weight lack the ability to penetrate breastmilk (Dalal et al., 2014). Drugs during the perioperative period can be classified into standard pharmacological categories of analgesic opioids, benzodiazepines, intravenous anesthetic agents, local anesthetics, neuromuscular blockers and reversal agents, and volatile anesthetic.

Analgesic opioids. Judicious administration of analgesic opioids in the perioperative period is a requisite for anesthetic practice due to their risk of maternal and infant respiratory depression, hypercapnia, and hypoxemia. Discussion of commonly used opioids, their transfer into breastmilk, and recommendations are below.

Fentanyl. Favored for its short duration of action and fast onset, Fentanyl is one of the most commonly administered opioids utilized for analgesia during the perioperative period. Authors established that maternal administration of fentanyl in the perioperative period was unlikely to result in adverse outcomes for a healthy, term breastfeeding infant and no requirement for milk discarding or waiting for the resumption of breastfeeding is required (Nitsun et al., 2006, Shergill et al., 2012).

Remifentanil. Remifentanil may be a promising perioperative opioid analgesic for breastfeeding mothers due to its unique pathway of metabolism in the serum, rapid onset and offset, lack of accumulation and rapid recovery after discontinuation of its administration (Flood et al., 2015). Four case studies presented by Stuttmann, Schafer, & Hilbert (2010) reported no adverse outcomes or signs of sedation in breastfeed infants after maternal administration of remifentanil as part of their general anesthetic. However, remifentanil is an unsuitable option for the treatment of acute postoperative pain due to its brief context-sensitive half-life of less than 10 minutes.

Morphine. Considered less potent when compared to Fentanyl, Morphine is a commonly used opioid in anesthetic practice favored for its longer duration of action and treatment of postoperative pain reaching peak effect 90 minutes after intravenous administration (Flood et al., 2015). However, morphine is associated with a greater depression of ventilatory response to hypoxia in women. Metabolized to an active, more potent metabolite Morphine-6-glucurcoids requires renal elimination (Flood et al., 2015). Morphine secretion in breastmilk was studied in the literature over two decades ago. Earlier studies suggest that the amount of maternally transferred morphine to the breastfeeding infant is variable and warrants caution (Robieux et al., 1990, Baka et al., 2002). Furthermore, infants under one month of age, exposed to morphine are at an increased risk of sedation and respiratory problems due to immature metabolization and clearance of the drug (Hale, 2017). Evidence suggests that morphine administration to the breastfeeding mother should be avoided or used with extreme caution with the close infant and maternal monitoring (Dalal et al., 2014).

Other. Current literature suggests that perioperative administration of other analgesic opioids such as meperidine and hydromorphone are not of the agents of choice in lactating women as there is an increased risk of respiratory depression for the breastfeeding infant (Dalal et al., 2014).

Benzodiazepines. Midazolam is one of the most common benzodiazepines administered as part of a general anesthetic for its sedating and anxiolytic effects. Several authors suggest that midazolam administered perioperatively was not likely to affect a healthy, term infant which supports the resumption of breastfeeding after surgery (Nitsun et al. 2006, Dalal et al. 2014). The use of perioperative diazepam or lorazepam is considered unsafe for the breastfeeding infant and should be avoided.

Intravenous anesthetic agents. General anesthesia is induced by administration of intravenous anesthetic agents, which cause a reversible loss of consciousness. Commonly used intravenous anesthetic agents include propofol, ketamine, & etomidate. Due to their short duration of action and rapid metabolism with no active metabolite, propofol and etomidate are considered safe for administration in the breastfeeding mother with no waiting period necessary for the resumption of breastfeeding (Cobb et al., 2015). The combined administration of ketamine & propofol has been shown to decrease postoperative pain and opioid consumption in breastfeeding mothers (Jaafarpour, Vasigh, Khajavikhan, & Khani, 2017). Research literature regarding ketamine is not existent. Ketamine's short half-life and rapid redistribution out of plasma suggest milk levels of ketamine would be low after maternal administration (Hale, 2017, LactMed®, 2017). Current recommendations include close infant monitoring after maternal administration.

Local anesthetics. Local anesthetics physiochemical properties limit their ability to transfer into breastmilk and furthermore are poorly absorbed by the breastfeeding infant (Chu et al., 2013, Cobb et al., 2015). Authors established that intravenous, peripheral, or neuraxial administration of lidocaine results in minimal lidocaine concentrations in breastmilk, is not

expected to cause adverse effects in the nursing infant, and reduces postoperative opioid requirements for nursing mothers (Chu et al., 2013, Cobb et al., 2015, Thawart et al., 2016). Neuraxial administration of lidocaine, bupivacaine, or ropivacaine is safe to use in lactating women, and no special precautions are required (Cobb et al., 2015, Dala et al., 2013).

Neuromuscular blockers and reversal agents. General anesthesia often requires neuromuscular relaxation to facilitate ease of endotracheal intubation and a favorable surgical environment. Chemical properties inherent to neuromuscular blocking agents; large molecular size, poor lipid solubility, and polarized nature restrict their ability of passively diffuse into breastmilk and are presumed safe for use in lactating women (Dala et al., 2014, Chu et al., 2013, Cobb et al., 2015). Also, the rapid metabolization and poor oral bioavailability of commonly used neuromuscular blocking agents; succinylcholine, vecuronium, rocuronium, and cisatracurium, demonstrates the unlikelihood of these agents to reach breastmilk in sufficient concentrations or reach the bloodstream of a breastfeeding infant (Dala et al., 2014). The combination of an acetylcholinesterase-inhibiting agent (neostigmine) and an anticholinergic agent (glycopyrrolate) is often given to reverse neuromuscular relaxation. As quaternary ammonium compounds, glycopyrrolate and neostigmine, physiochemical properties prevent their ability to penetrate the blood-milk barrier easily and are unlikely to affect the breastfed infant (Dala et al., 2014, Cobb et al., 2015, LactMed®, 2017)

Inhaled anesthetics. There is no published data in regards to inhaled anesthetic levels measured in human milk. Inhaled anesthetics have poor bioavailability and are rapidly eliminated once administration ceases via alveolar ventilation (Flood et al., 2015). Based on the available evidence and known pharmacokinetics of the elimination of inhaled anesthetics, absorption by the breastfeeding infant is likely nil and no discarding of milk or waiting period is required (Bhaskara et al., 2016, Dala et al., 2014, Reece-Stremtan, Campos, & Kokajko, 2017).

Antiemetics. Ondansetron and metoclopramide are commonly used agents for the prevention and treatment of postoperative nausea and vomiting. As well, these agents have been used in lactating women for treatment of nausea after cesarean section (ondansetron) and as galactagogues (metoclopramide) (LactMed®, 2017). Ondansetron and metoclopramide readily cross the blood-milk barrier, no adverse infant effects have been reported and may be safely used in lactating women (Dala et al., 2014, Chu et al., 2013, Elkomy et al., 2015).

Anesthesia resource

Anesthesia Providers Quick Guide for the Breastfeeding Mother

A breastfeeding mothers return to baseline mentation & strength, suggests drug redistribution from plasma and milk, and termination of drug action (Cobb et al., 2015).

	Proceed	Caution	AVOID	
Analgesic Opioids *(Lowest dose possible to achieve adequate analgesia)*	Fentanyl Remifentanil Alfentanil	Morphine	Meperidine Hydromorphone	
Benzodiazepines	Midazolam	-	Diazepam Lorazepam	***When administering a combination of anesthetic agents, follow the recommendations for the most problematic medication used during the procedure and caution is advised for anesthetic agents with prolonged half-lives and potent metabolites that may lead to drug accumulation (LactMed®, 2017, Sachs, 2013, Shergill et al., 2012).***
Intravenous Anesthetic Agents	Propofol Etomidate	Ketamine	-	
Local Anesthetics	Lidocaine Bupivacaine Ropivacaine	-	-	
Neuromuscular Blockers	Succinylcholine Rocuronium Vecuronium Cisatracurium	-	-	
Neuromuscular Blocker Reversal Agents	Neostigmine/ Glycopyrrolate Atropine	-	-	***As a general principle, one a mother has recovered from general anesthesia, mothers can resume breastfeeding, with NO required waiting period or discarding of milk necessary (Chu et al., 2013, Dalal et al. 2014, Kelly et al., 2012, Shergill et al., 2012).***
Inhaled Anesthetics	Isoflurane Sevoflurane Desflurane	-	-	
Antiemetics	Ondansetron Dexamethasone Metoclopramide	-	-	

Implications for clinical practice and research

Limitations identified in the literature search was a narrow pool of current high-level research studies, finding that most notable and established studies concerning breastfeeding and anesthetic agents were published over a decade earlier. Do to ethical constraints and the considerably small population of breastfeeding mothers who require general anesthesia; there is a scarcity of large or robust studies in this population. Current scientific literature is limited to observational studies, retrospective cohort studies, case studies, and literature reviews focusing on pharmacological properties of anesthetic agents (Dalal et al., 2014, Kelly et al., 2012, Nitsun et al., 2006, & Shergill et al., 2012).

Lack of robust studies with randomization, small sample size, and limited sample settings that predominate current literature challenges credibility and can undermine transferability of current research. Additionally, gaps identified include lack of human data, specifically studies that detect the presence of many commonly used anesthetic agents in breastmilk (e.g., ketamine, sevoflurane, remifentanil). Not found in the literature are studies that evaluate the transfer of drugs via breastmilk to children that may reveal different pharmacodynamic profiles since there is an increased amount of breastmilk consumption and therefore drug ingestion in this population (Chu et al., 2013). Due to the fragility of premature and special

needs infants, there is limited information in regards to recommendations for resumption of breastfeeding in this distinctive population.

Conflict of interests

The author of this CPG certifies that there has been no competing interests or compromise in the editorial independence of the developed CPG. No financial compensation or funding has been received for the development of this CPG. In partial fulfillment of the degree of Doctorate of Nursing Practice, this CPG has been developed with no conflict of interest to report.

APPENDIX E:

SYNTHESIS OF EVIDENCE

Author (Year)	Research Question	Study Design/Framework	Sample and Setting	Data Collection (Instruments/tools)	Findings
Dozier, A., Howard, C., Brownell, E., Wissler, R., Glantz, J., Ternullo, S, & Lawrence, R. (2013)	A potential association between intrapartum epidural anesthesia use and overall breastfeeding cessation within one month postpartum	Mixed methods: retrospective chart review, bivariate retrospective chart review	**Sample:** 727 healthy mothers (>18 y/o age) from 2 cohorts w/ healthy term singleton vaginal delivers who had initiated breastfeeding **Setting:** Three community hospitals in upstate New York	Medical record data abstracted from EHR & maternal self-report via survey @ 2-weeks & 3-months postpartum.	Epidural anesthesia significantly predicted breastfeeding cessation (hazard ratio 1.26 [95 % confidence interval 1.10, 1.44], $p < 0.01$) Low income, less education, and no breastfeeding goal predicted early cessation
Dalal, P., Bosak, J. & Berlin, C. (2014)	Safety of anesthesia-related drugs in lactating women and their potential effects on the breastfed infant.	Literature review	A search of available literature was conducted using the PubMed database from the National Library of Medicine, and LactMed Website. Researched commonly used drugs used in the perioperative period: anesthetic drugs,	Reviewed articles were graded based on the Levels of Evidence (LOE) and the strength of recommendation (SOR) grading followed by the Oxford Center for Evidence Based medicine.	Adverse drug reactions in breastfed infants following maternal drug exposure are rare; most being minor incidents and notably in infants <2 months of age. Drugs are transferred into breastmilk, the amount transferred is clinically insignificant and poses minimal to no risk to the nursing infant.

Author (Year)	Research Question	Study Design/Framework	Sample and Setting	Data Collection (Instruments/tools)	Findings
Kelly, L., Poon, S., Madadi, P., & Koren, G. (2012)	Assess CNS depression and other adverse effects in infants exposed to benzodiazepines through breastmilk.	Prospectively recruited, retrospectively assessed cohort study of mothers	One hundred twenty-four self-referred mothers who contacted a local hospital in Toronto, Ontario between January 2010 & May 2011 for advice regarding the use of benzodiazepines during lactation. **Inclusion criteria:** Fluent English speaking Used Benzodiazepines during breastfeeding.	Breastfeeding follow-up form via telephone interview. Intake forms included: Medication used Frequency of breastfeeding Health of infants Demographic characterizes Categorical data for infant obtained during follow up included: Maternal & infant health concerns, evidence of neonatal CNS depression, breastfeeding frequency. Significance critical value of $P < 0.5$ was set	Sedation was identified in 1.6 % of infants, and was not associated w/ benzodiazepine dose, the number of hours breastfeeding or taking concomitant CNS depressants. **Conclusion:** Supports the continued breastfeeding while taking benzodiazepines post-partum.
Nitsun, M., Szokol, J., Saleh, H., Murphy, G., Vender, J., Luong, L., & Avram, M. (2006)	Determine the pharmacokinetics of midazolam, Propofol, & fentanyl transfer into milk.	Quasi-experimental observational study	Five lactating women who required general anesthesia Premedicated w/ midazolam before induction of anesthesia. Maintenance of anesthesia w/ potent volatile anesthetic	Milk & blood collected before drug administration. Milk collected 5, 7, 9, 11, & 24 hours after drug administration. Venous blood was collected at intervals up to 7 hours post drug administration. Plasma & mild midazolam, Propofol, & fentanyl concentrations measured	24 hour milk collection averages: •**Midazolam:** 0.005 % of maternal dose. •**Propofol:** 0.027 % of maternal dose. •**Fentanyl:** 0.033 % of maternal dose **Conclusion:** The amount of drug excreted into milk w/ in 24 hours of induction of anesthesia is not

Author (Year)	Research Question	Study Design/Framework	Sample and Setting	Data Collection (Instruments/tools)	Findings
				by HPLC w/ tandem mass spectrometry & florescence detection.	sufficient enough to justify the interruption of breastfeeding.
Bhaskara, B., Dayananda, V., Kannan, S., Rao, R. R., & Ramachandraiah, R. (2016)	Assess the effects of breastfeeding on the consumption of Propofol, sevoflurane, and hemodynamic stability in women	A single-blind, prospective study	One hundred twenty women scheduled for tubectomy under GA. **Demographics:** ASA class I & II Ages 20-30 y/o Uncomplicated pregnancy Delivered full-term healthy infants by vaginal route. Random allocation of study participants into three groups (40 in each group) (1) Breastfeeding (BF) (2) Withhold feeding (WF) (3) Non-feeding (NF) group.	HR, MAP, and state entropy (SE) values recorded @ regular intervals. All participates received induction w/ propofol, maintenance of anesthesia w/ sevoflurane, in 60% N2O & O2 mixture. Analysis of variance & Chi-square test utilized for analysis of results	BF group demonstrated: Reduces consumption of propofol by 20% & reduced consumption of sevoflurane by 35 % ($p<0.05$) when compared to NF group. Persistently low HR & MAP compared to WF group ($P < 0.05$) Conclusion: BF before induction of anesthesia decreases consumption of sevoflurane & propofol, and preserves hemodynamic stability.
Shergill, A., Ben-Menachem, T., Chandrasekhara, V., Chathadi, K., Decker,	Guideline for educational purposes to provide information that will assist endoscopists in	Clinical Guideline	Updated guideline utilizing PubMed for a search of medical literature. Additional	Reviewed articles are graded on the strength of the supporting evidence. The power of individual	Midazolam – recommendation to withhold nursing of the infant for @

Author (Year)	Research Question	Study Design/Framework	Sample and Setting	Data Collection (Instruments/tools)	Findings
G., Evans, J., Early, D., Fanelli, R., Fisher, D., Foley K., Fukami, N., Hawang, J., Jain, R., Jue, T., Khan, K., Lightdale, J., Pasha, S., Sharaf, R., Dominitz, J., & Cash, B.,(2012)	providing care to breastfeeding patients		references were obtained from the bibliographies of the identified articles. Recommendations of expert consultants are included as well.	recommendations is based on aggregate evidence & assessment of the anticipated benefits & harms.	least 4 hours following administration Fentanyl – is compatible with breastfeeding. Meperidine – compatible w/ breastfeeding, however alternative such as fentanyl is preferred. Propofol no interruption of breastfeeding recommended
Sachs, H. C. (2013).	Discussion regarding topics of interest surrounding lactation	A clinical report from the American Academy of Pediatrics	Update on the transfer of drugs and therapeutics into human breastmilk, the expert option of authors	Clinical report discussing lactation & the use of psychotropic therapies, drugs to treat substance abuse, narcotics, galactagogues, herbal produces, & immunizations of breastfeeding women.	Caution is advised for the use of codeine & hydrocodone in both mother & nursing infant. Benefits of breastfeeding outweigh the risk of exposure to most therapeutic agents via breastmilk.

Author (Year)	Research Question	Study Design/Framework	Sample and Setting	Data Collection (Instruments/tools)	Findings
Reece-Stremtan, S., Campos, M., & Kokajko, L. (2017)	Guidelines for the care of breastfeeding mothers & infants focus on anesthesia & analgesia for breastfeeding mothers outside the postpartum period.	Clinical protocol	A search of available literature as well as up-to-date information about specific medications from LactMed and other internet-based websites.	Appraisal of current evidence and information about medications pharmacologic properties, milk levels and rare infant effects in case reports. Quality of evidence leveled based on National Guidelines Clearing House	Resumption of normal mentation in the mother of a healthy term or older infant can resume breastfeeding with no interruption. Interruption of breastfeeding (6-12) hours may be advised for infants at risk for apnea, hypotension, or hypotonia after maternal anesthesia.
Kutlucan, L., Seker, I., Demiraran, Y., Ersoy, O., Karagoz, I., Sezen, G., & Kose, S. A. (2014)	Is there a delay in the onset of lactation in patients undergoing cesarean section w/ general anesthesia when compared w/ patients who undergo cesarean section w/ spinal & epidural anesthesia and with patients who undergo normal vaginal birth?	Randomized cohort study	84 patients, 18-40 years of age, ASA I-II **Four groups** G – general anesthesia n:21 S – spinal anesthesia n:21 E – epidural anesthesia n:21 V – vaginal birth w/ out anesthesia n:21	Pre & post procedure oxytocin & prolactin values were measured	No significant differences amount hormone levels in the postpartum period (9=0.350) General anesthesia w/ propofol administration was associated w/ increased oxytocin hormone level. General anesthesia is associated w/ a delay in the start of lactation (p=0.003)

Author (Year)	Research Question	Study Design/Framework	Sample and Setting	Data Collection (Instruments/tools)	Findings
Jaafarpour, M., Vasigh, A., Khajavikhan, J., & Khani, A. (2017)	Assess the effect of ketofol (ketamine/propofol combination) on pain & complications after caesarian delivery under spinal anesthesia and interference w/ breastfeeding	Randomized double-blinded clinical trial	92 parturient scheduled for elective cesarean delivery under spinal anesthesia Four groups: 1-ketamine 0.25 mg/kg 2-propofol 0.25 mg/kg 3-ketofol (25 mg ketamine + 25 mg propofol) 4- placebo saline	Drugs administered immediately after clamping the umbilical cord. Visual Analog Scale (VAS) was used to determine the intensity of pain. SPSS used for data analysis, descriptive statistics, one-way ANOVA, least significant difference (LSD) test & repeated measurements was carried out. $P < 0.05$ was considered as significant	Administration of ketofol was associated w/ reduce pain & complications after cesarean delivery and can be considered a safe & alternative drug for lactating women. Morphine consumption, the mean score of pain, & time of breastfeeding was significantly lower in patients who received ketofol

APPENDIX F:

EDUCATIONAL PAMPHLET

Anesthesia Providers Quick Guide for the Breastfeeding Mother

A breastfeeding mothers return to baseline mentation & strength, suggests drug redistribution from plasma and milk, and termination of drug action (Cobb et al., 2015).

	Proceed	Caution	AVOID
Analgesic Opioids *(Lowest dose possible to achieve adequate analgesia)*	Fentanyl Remifentanil Alfentanil	Morphine	Meperidine Hydromorphone
Benzodiazepines	Midazolam	-	Diazepam Lorazepam
Intravenous Anesthetic Agents	Propofol Etomidate	Ketamine	-
Local Anesthetics	Lidocaine Bupivacaine Ropivacaine	-	-
Neuromuscular Blockers	Succinylcholine Rocuronium Vecuronium Cisatracurium	-	-
Neuromuscular Blocker Reversal Agents	Neostigmine/ Glycopyrrolate Atropine	-	-
Inhaled Anesthetics	Isoflurane Sevoflurane Desflurane	-	-
Antiemetics	Ondansetron Dexamethasone Metoclopramide	-	-

When administering a combination of anesthetic agents, follow the recommendations for the most problematic medication used during the procedure and caution is advised for anesthetic agents with prolonged half-lives and potent metabolites that may lead to drug accumulation (LactMed®, 2017, Sachs, 2013, Shergill et al., 2012).

As a general principle, one a mother has recovered from general anesthesia, mothers can resume breastfeeding, with NO required waiting period or discarding of milk necessary (Chu et al., 2013, Dalal et al. 2014, Kelly et al., 2012, Shergill et al., 2012).

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